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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,356	10/06/2003	Chiaki Ishii	58600-8229.US00	5651
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King & Spalding LLP P.O. Box 889 Belmont, CA 94002-0889			EXAMINER POPA, ILEANA	
			ART UNIT 1633	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/680,356	<b>Applicant(s)</b> ISHII ET AL.	
	<b>Examiner</b> ILEANA POPA	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 March 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 6-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. Claims 5, 19, and 20 have been cancelled. Claims 13-18 and 21 have been withdrawn. Claims 1 and 8 have been amended.

Claims 1-4 and 6-12 are under examination.

2. All rejections pertaining to claim 5 are moot because Applicant cancelled the claim in the reply filed on 03/30/2009.

The rejections of claims 1-4, 9, 11, and 12 under 35 U.S.C. 102(b) as being anticipated by Boxer et al. (WO98/23948), of claims 1-4 and 9-12 under 35 U.S.C. 103(a) as being unpatentable over Boxer et al., in view of each Cornell et al. (U.S. Patent No. 5, 874,316) Arnold et al. (U.S. Patent 5, 310, 648), and Bayerl et al. (U.S. Patent No. 6,051,372), and of claims 1-4, 8, 9, 11, and 12 under 35 U.S.C. 103(a) as being unpatentable over Boxer et al., in view of Shen et al. (PGPUB 2003/0148335) are withdrawn in response to Applicant's amendment to claim 1 filed on 03/30/2009. Specifically, claim 1 was amended to recite that the biomolecule is a vesicle, limitation which is not taught by Boxer et al. or by the combination of Boxer et al. with Cornell et al., Arnold et al., and Bayerl et al. or with Shen et al.

### ***Response to Arguments***

### ***Claim Rejections - 35 USC § 103***

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3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-4, 6, 7, 9, 11, and 12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. (WO98/23948), in view of both Boukobza et al. (J Phys Chem, 2001, 105: 12165-12170) and Niemeyer (DE 19902391, Abstract).

Boxer et al. teach a surface detector array device comprising a substrate defining a plurality of distinct bilayer-compatible surface regions separated by one or more bilayer barrier regions, a bulk aqueous phase covering the substrate surface, a lipid bilayer expanse carried on each of the bilayer-compatible region, and an aqueous film interposed between each bilayer-compatible region and the corresponding lipid bilayer expanse, i.e., the aqueous film is interposed between the bilayer-compatible surface region and the lower surface of the corresponding bilayer expanse (claims 1 and 9) (p. 4, lines 5-12). Boxer et al. teach that the lipid bilayer expanses have different compositions (claim 3) (p. 4, lines 32 and 33). With respect to the limitation of inner and outer surfaces (claim 1), a bilayer lipid necessarily has inner and outer surfaces; therefore, Boxer et al. do teach lipid bilayer expanses with an inner and an outer bilayer surface (compare also Fig. 1 of the international publication WO98/23948 with Fig. 1 of the instant application, both depicting the same composition). Boxer et al. teach that the bilayer expanses may be modified so that they comprise lipids covalently coupled to

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biomolecules such as polynucleotides (i.e., oligonucleotide), wherein each bilayer expanse could have a specific biomolecule and wherein the biomolecules can be used to non-covalently attach other biomolecules to the bilayer via specific molecular interactions; i.e., Boxer et al. teach that biomolecules can be attached to the bilayer expanses via specific molecular interactions between complementary oligonucleotides, wherein each expanse comprises a specific oligonucleotide (claims 1 and 4) (p. 4 bridging p. 5, lines 1-5, p. 16, lines 3-21). The bilayer-compatible surface regions may be formed of materials such as  $\text{SiO}_2$ ,  $\text{MgF}_2$ ,  $\text{CaF}_2$ , and mica (claim 11) and the bilayer expanse may comprise phosphatidylcholine (claim 12) (p. 4, lines 13-15 and 20-24). Boxer et al. also teach that one embodiment relates to sorting devices for biomolecules integrated or attached to the supported bilayer, wherein the device comprises barrier regions acting as two dimensional sieves having progressively smaller openings that are capable to sort the membrane-associated molecule by size, i.e., the array comprises discrete bilayer patches associated with the lipid bilayer expanses (claim 2) (p. 25 bridging p. 26 and Fig. 5).

Boxer et al. do not teach the biomolecule being a vesicle or second biomolecules associated with the bilayer expanses wherein the second biomolecules are capable of freely moving within the expanse, nor do they teach some of the bilayer expanses as having different second molecules (claims 1, 6, and 7). However, at the time the invention was made, such was taught by the prior art. For example, Boukobza et al. teach a novel immobilization technique for biomolecules comprising trapping single protein molecules inside lipid vesicles (i.e., a first and a second biomolecule), which are

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tethered to a supported lipid bilayer via biotin-avidin interaction, wherein the technique overcomes the problem of molecule-surface interaction and wherein the surface-tethered vesicles can be used for experiments on reconstituted membrane proteins and peptides (i.e., a vesicle capable of specifically binding a test agent) (claims 1 and 6) (p. 12165, column 2, second paragraph, p. 12166, column 1, Fig. 1, p. 12169, column 2, *Conclusion*). It would have been obvious to one of skill in the art, at the time the invention was made, to use the oligonucleotide hybridization as taught by Boxer et al. to tether vesicles to the array of separated lipid bilayers, with a reasonable expectation of success. One of skill in the art would have been motivated to do use oligonucleotides for tethering in order to obtain expanses with different vesicle composition, each vesicle being encoded by a specific oligonucleotide, as needed. One of skill in the art would have been expected to have a reasonable expectation of success in doing so because the prior art teaches that oligonucleotides are versatile and their use allows for the parallel immobilization of different macromolecules coupled to different nucleic acids (see Niemeyer, Abstract). One of skill in the art would have been motivated to tether vesicles to the array of Boxer et al. because Boukobza et al. teach that vesicles are more suitable than the planar bilayers for studying functional membrane dynamic. With respect to the limitation recited in claim 6, absent evidence of the contrary the protein-loaded vesicles are able to freely move within the expanse. With respect to the limitation recited in claim 7, one of skill in the art would have been motivated to use different second molecules in order to study the reconstitution of several membrane proteins at the same time.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Applicant traversed the instant rejection on the grounds that the combination of Boxer et al., in view of both Boukobza et al., and Niemeyer fails to teach or suggest the claimed invention because: **(i)** Boxer et al. do not mention the biomolecule being a vesicle, **(ii)** Boukobza et al. teach surface-tethered vesicles which encapsulate proteins and do not mention vesicles capable of specifically binding a test agent, and **(iii)** Niemeyer does not mention vesicles, anchoring via complementary oligonucleotides or lipids derivatized with a surface region specific oligonucleotide. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

Although Applicant argues that the combination of references cited above does not render his invention *prima facie* obvious, Applicant did not address the combination of references. Instead, Applicant argues the references individually. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). None of the cited references has to teach each and every claim limitation. If they did, this would have been anticipation and not an obviousness-type rejection. Applicant also argues

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that Boukobza et al. do not mention vesicles capable of specifically binding a test agent.

This is incorrect. As indicated in the rejection above, Boukobza et al. teach that the surface-tethered vesicles can be used for experiments on reconstituted membrane proteins and peptides, i.e., they teach that the vesicles are capable of specifically binding proteins as test agents.

Therefore, Applicant failed to show why the claimed invention is not rendered *prima facie* obvious by the combination of the cited references and the rejection is maintained.

### ***New Rejections***

#### ***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 1-4, 6, 7, and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. taken with both Boukobza et al. and Niemeyer, in further view of each Cornell et al. (U.S. Patent No. 5, 874,316, of record), Arnold et al. (U.S. Patent 5, 310, 648, of record), and Bayerl et al. (U.S. Patent No. 6,051,372, of record).

The teachings of Boxer et al., Boukobza et al., and Niemeyer are applied as above for claims 1-4, 6, 7, 9, 11, and 12.



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Boxer et al., Boukobza et al., and Niemeyer do not teach the use of self-limiting lateral diffusion to separate the lipid regions from one another (claim 10). However, at the time the invention was made, self-limiting lateral diffusion to separate the lipid regions from one another was taught by the prior art. For example, Cornell et al. teach receptor membranes, wherein the monomers in the membrane may be prevented from diffusing laterally by selecting lipids that are crystalline at room temperature, which eliminates lateral diffusion (column 3, lines 25-29). Arnold et al. teach an imprinted matrix, wherein the spatial organization of molecules in the substrate can be locked into place by a variety of means to form a structure incapable of lateral diffusion, for example by decreasing fluidity (column 7, lines 11-24, column 8, lines 1-10). Bayerl et al. teach patterned surfaces, wherein the lateral diffusion can be prevented by switching the lipid bilayer phase to gel or crystalline and wherein the phase transition can be accomplished by adjusting one physical parameter, the temperature (column 4, lines 25-58, column 5, lines 4-25, column 7, lines 1-24, column 9, lines 32-53). It would have been obvious to one of skill in the art, at the time the invention was made, to maintain the substrate orientation by limiting the lateral diffusion as taught by Cornell et al., Arnold et al., or Bayerl et al., with a reasonable expectation of success. One of skill in the art would have been motivated to do so because the prior art teaches that the use of self-limiting lateral diffusion to keep the lipid regions apart obviates the need for physical barriers on the substrate surface. One of skill in the art would have been expected to have a reasonable expectation of success in using any of the above-mentioned

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techniques because the art teaches the successful use of such techniques to limit lateral diffusion between discrete lipid regions.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

7. Claims 1-4, 6-9, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. taken with both Boukobza et al. and Niemeyer, in further view of Shen et al. (PGPUB 2003/0148335, of record).

The teachings of Boxer et al., Boukobza et al., and Niemeyer are applied as above for claims 1-4, 6, 7, 9, 11, and 12.

Boxer et al., Boukobza et al., and Niemeyer do not teach the identity of the biomolecule being determined from the sequence of the oligonucleotide (claim 8). Shen et al. teach the use of oligonucleotide identification tags for assaying the identity of non-nucleic acid targets, wherein the method can be used to identify any non-nucleic acid target associated with any surface (Abstract, p. 2, paragraphs 0009 and 0012, p. 3, paragraph 0017). Shen et al. teach that the oligonucleotide tag can be identified without dissociation by hybridization analysis, wherein the tag is detected by contacting it with an array of complementary nucleic acids immobilized on a support (p. 3, paragraphs 0021 and 0023). Therefore, it would have been obvious to one of skill in the art, at the time the invention was made, to determine the identity of the biomolecule from hybridization analysis of its attached oligonucleotide with the complementary oligonucleotide present on the bilayer expanse, as taught by Shen et al. with a

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reasonable expectation of success. One of skill in the art would have been expected to have a reasonable expectation of success in using such a method because the art teaches the successful use of oligonucleotide hybridization in determining the identity of oligonucleotide-tagged biomolecules.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

### **Conclusion**

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/  
Primary Examiner, Art Unit 1633